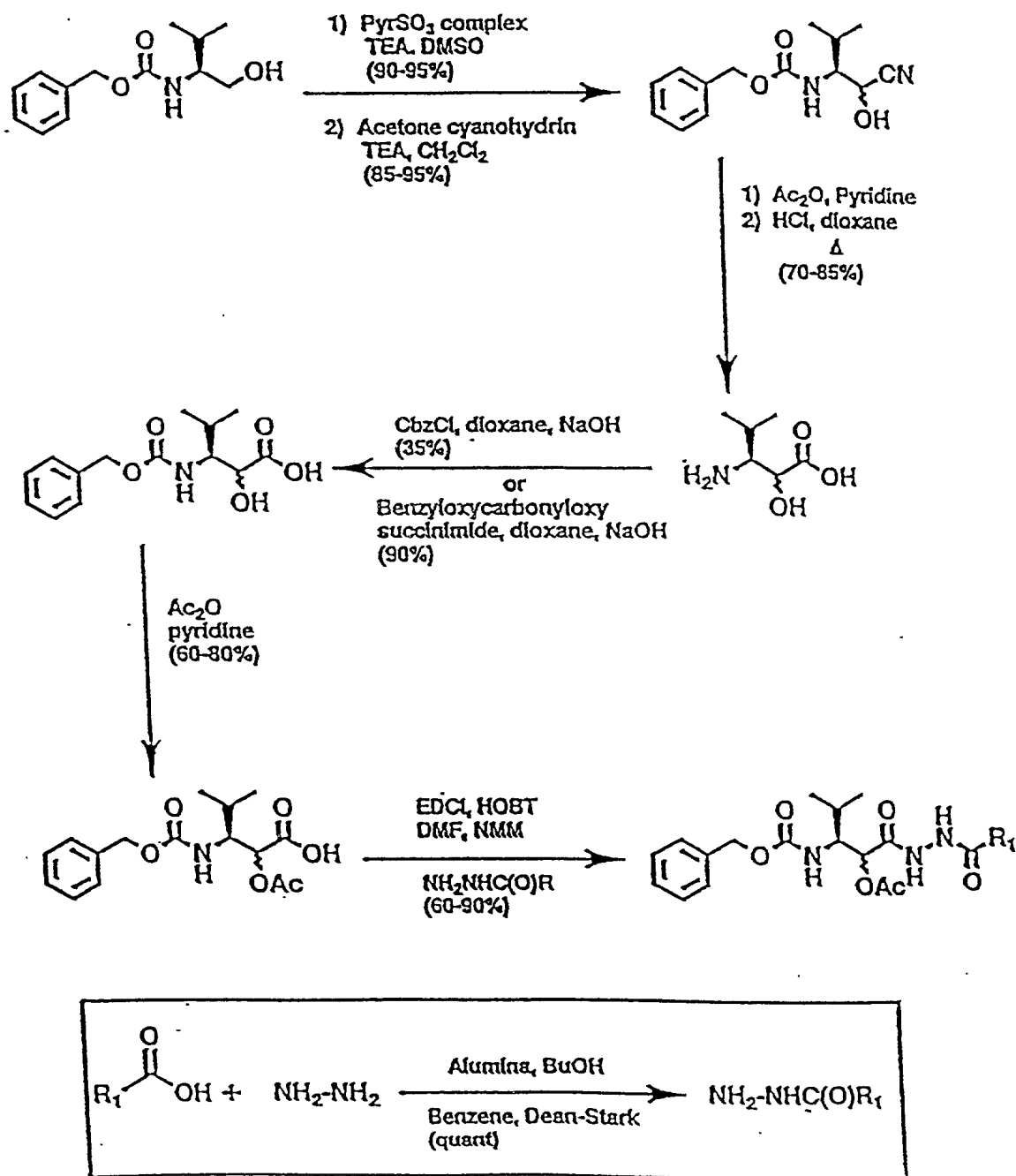


Figure 1

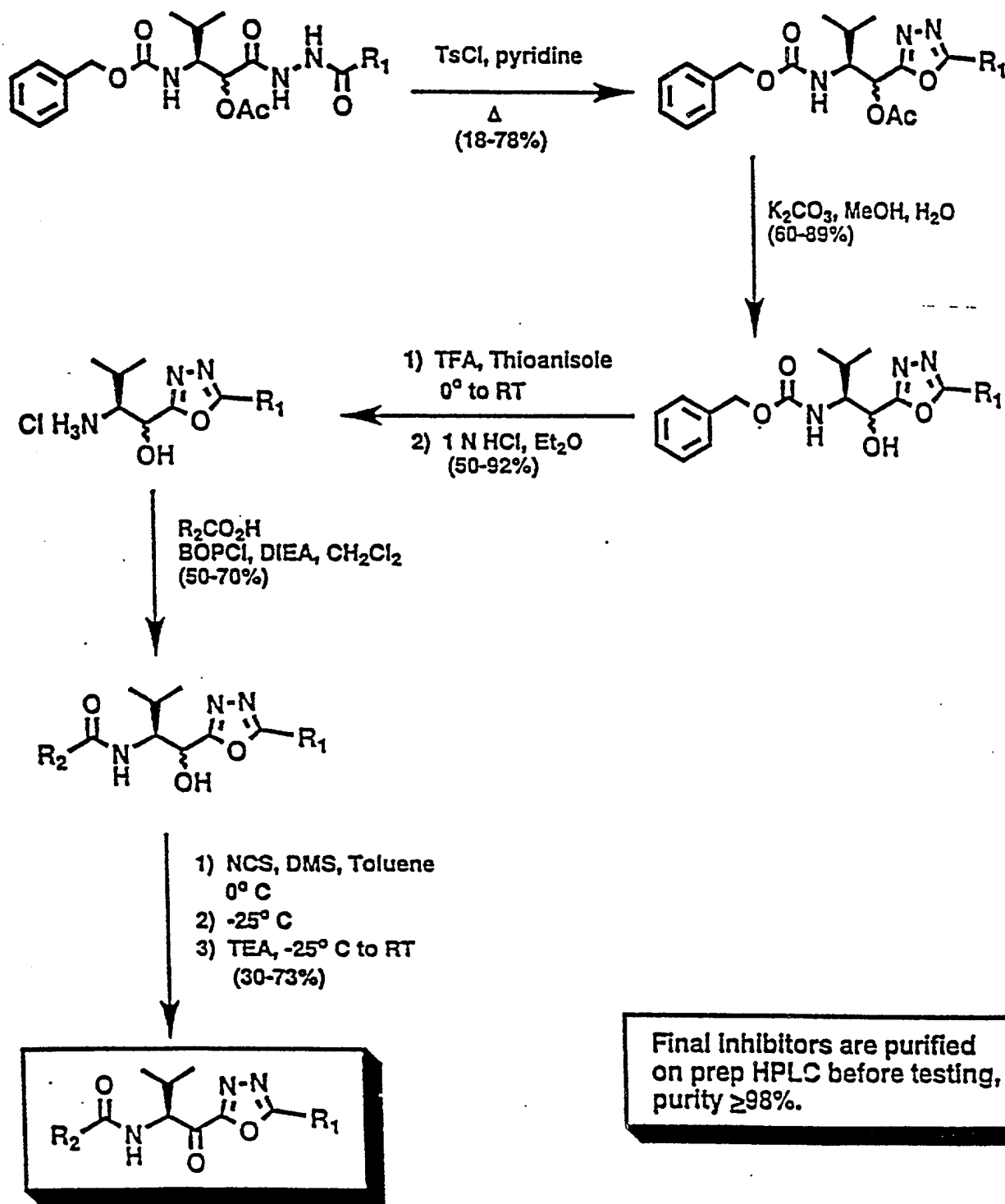
General Synthetic Scheme for 1,3,4-Oxadiazole Inhibitors



09927832-022202

Figure 2

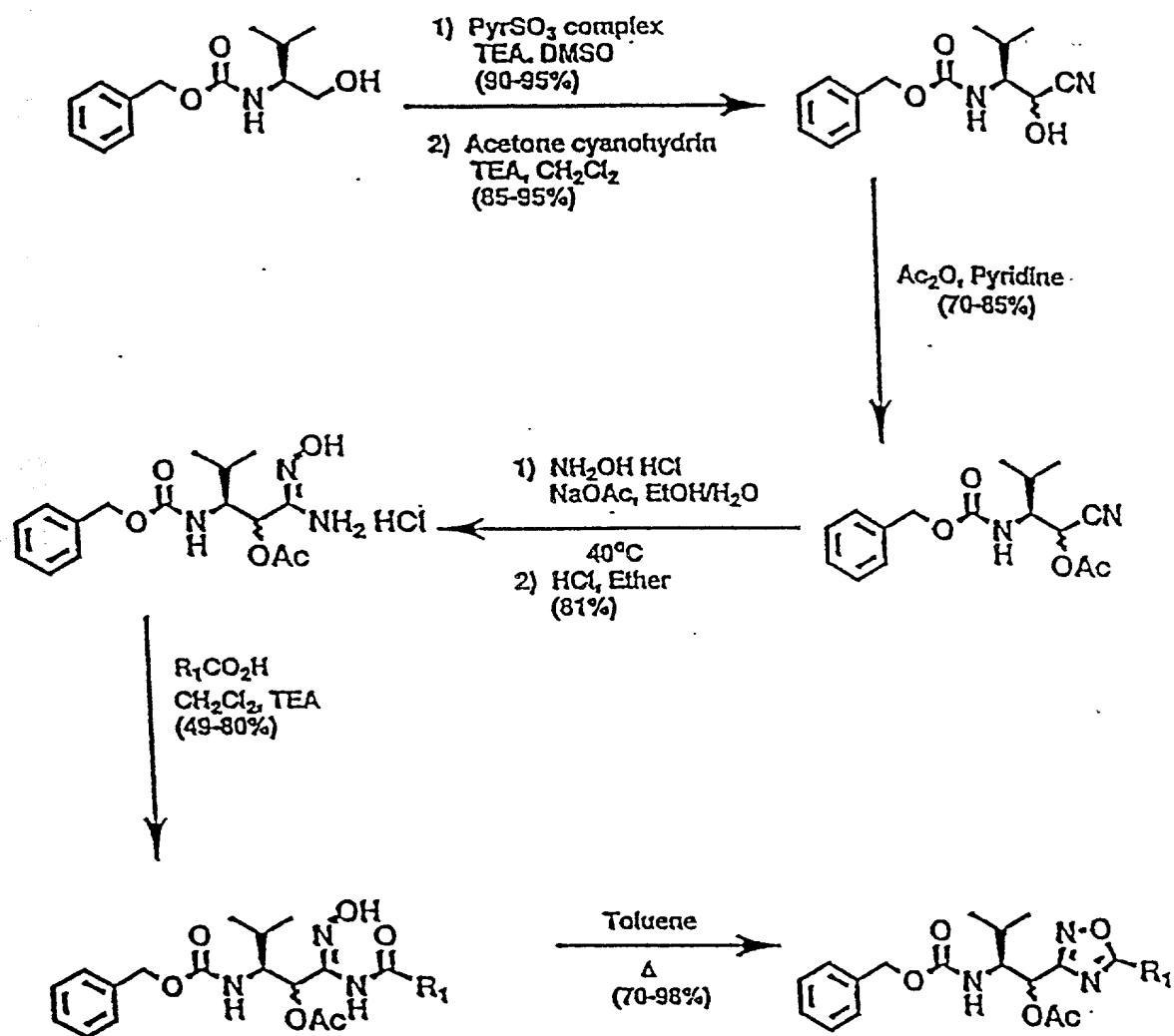
General Scheme for 1,3,4-Oxadiazole Inhibitors - Continued



09927833-022202

Figure 3

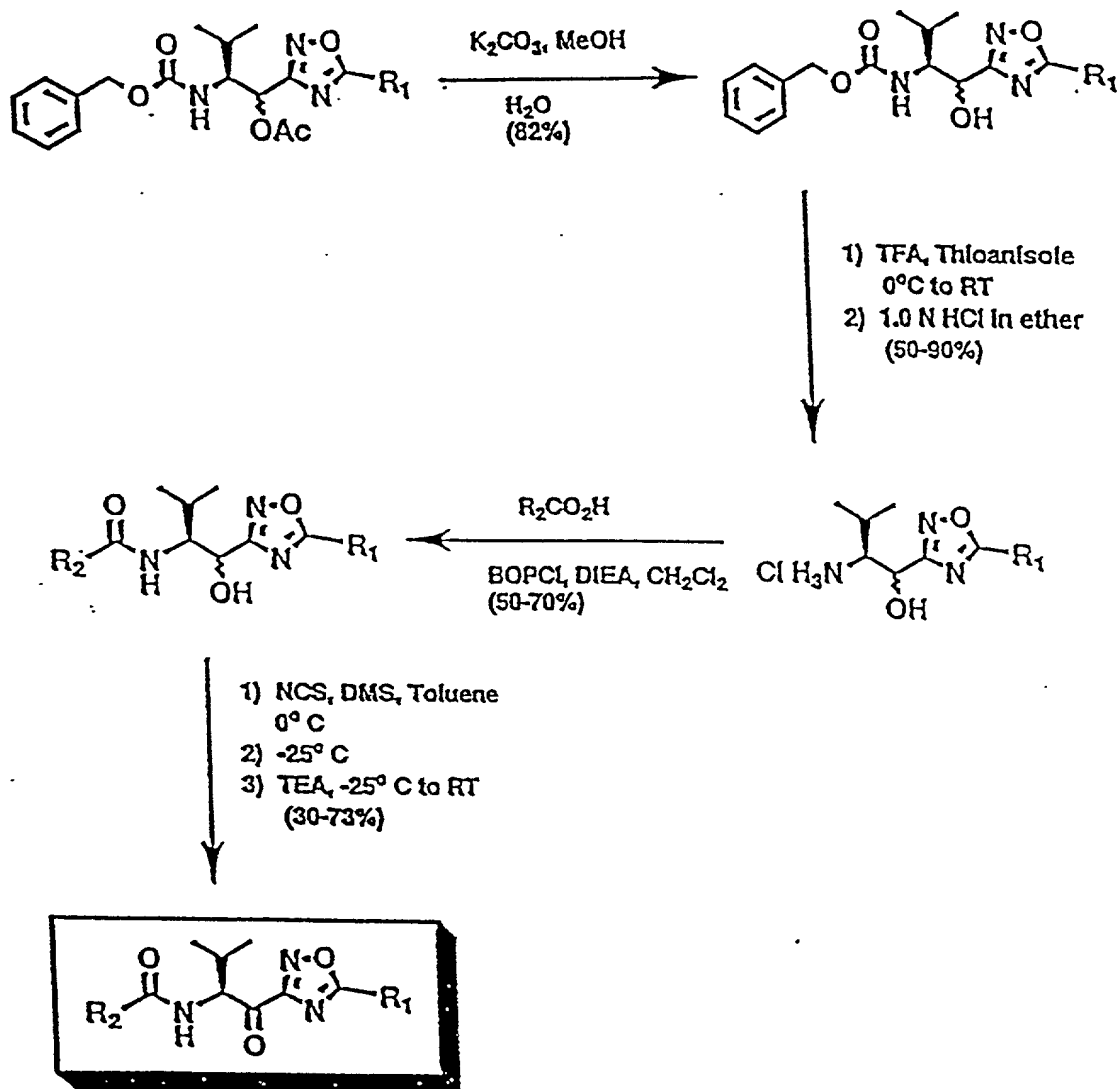
General Synthetic Scheme for 1,2,4-Oxadiazole Inhibitors



09927832-02302

Figure 4

General Synthetic Scheme for 1,2,4-Oxadiazole inhibitors
(Continued)



09927832-02202

Figure 5

General Synthetic Scheme for P₂-P₃ Modified Based Inhibitors

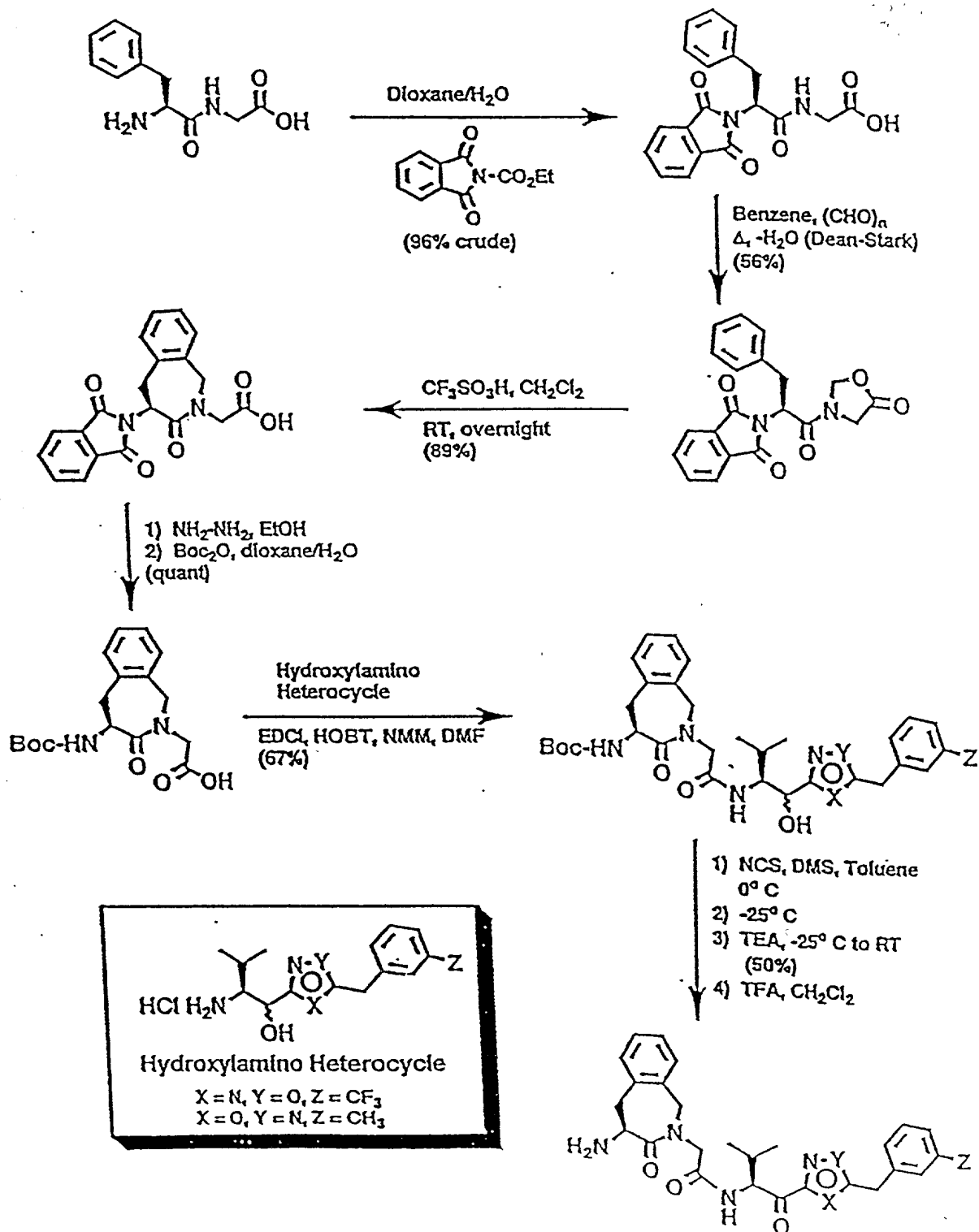


Figure 6

Synthetic Scheme for P₂-P₃ Modified Inhibitors

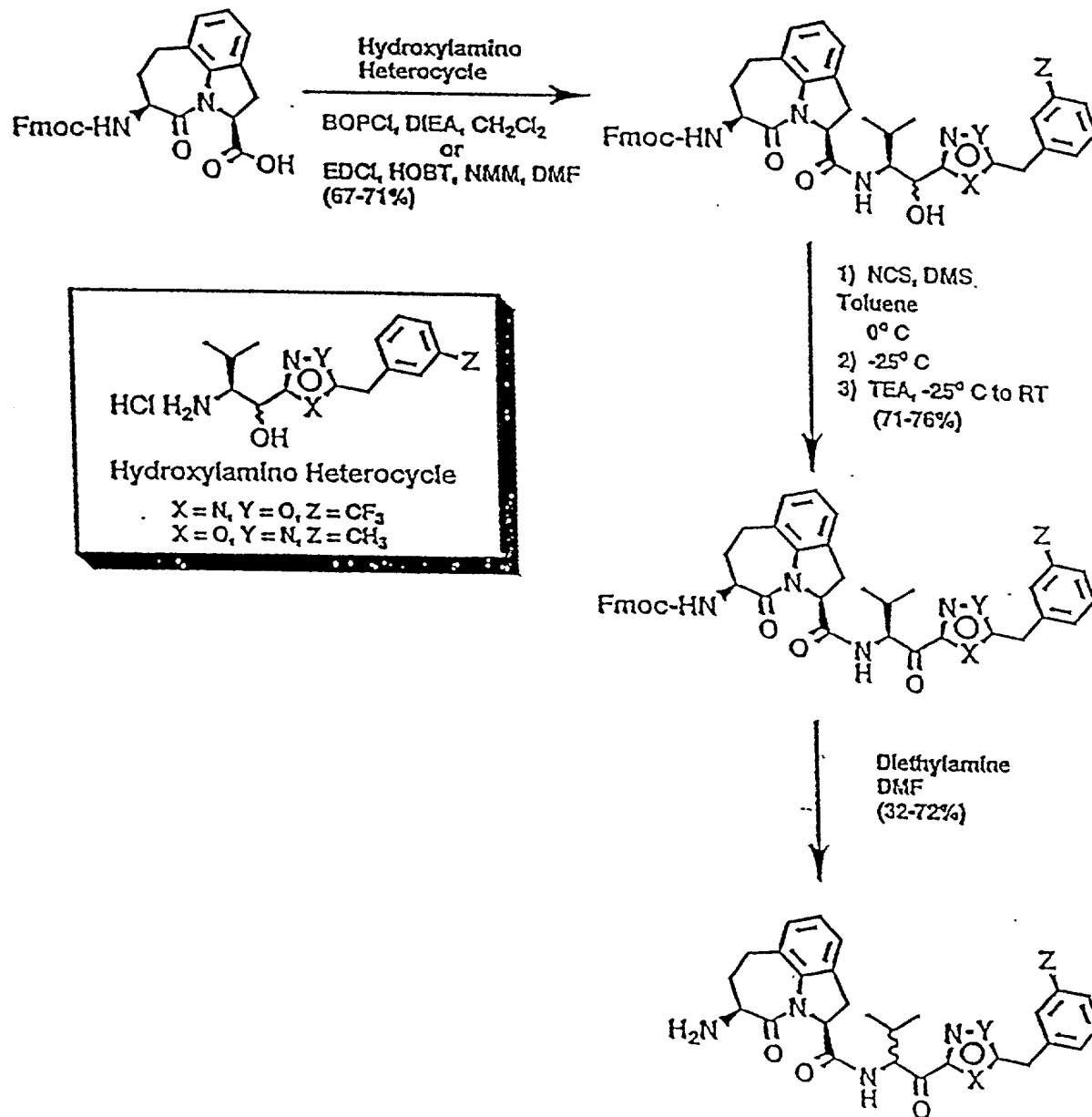


Figure 7

Synthetic Scheme for P₂-P₃ Modified Inhibitors

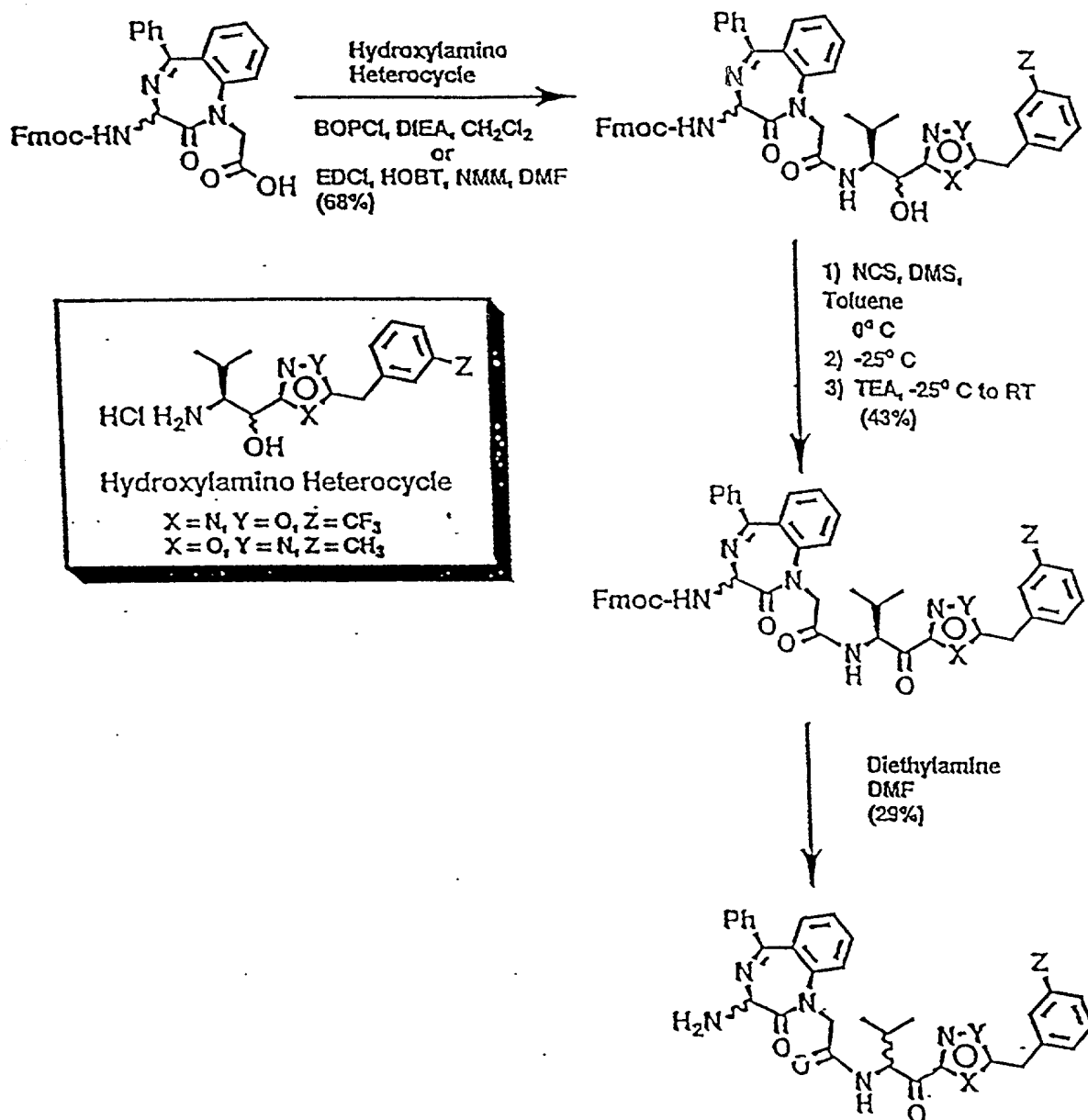


Figure 8

General Synthetic Scheme for P₂-P₃ Modified Inhibitors

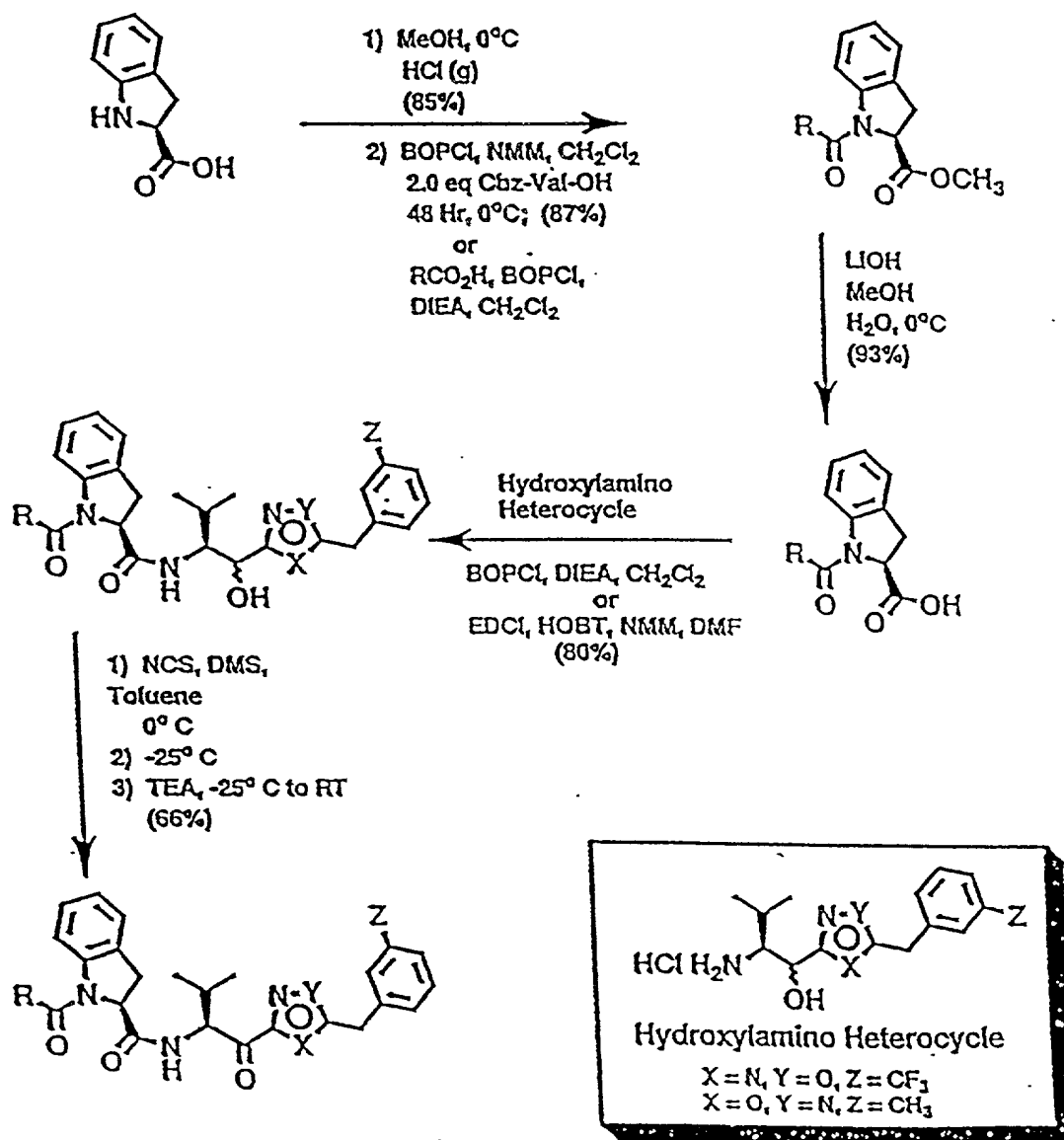


Figure 9

Synthetic Scheme for P₂-P₃ Modified Inhibitors

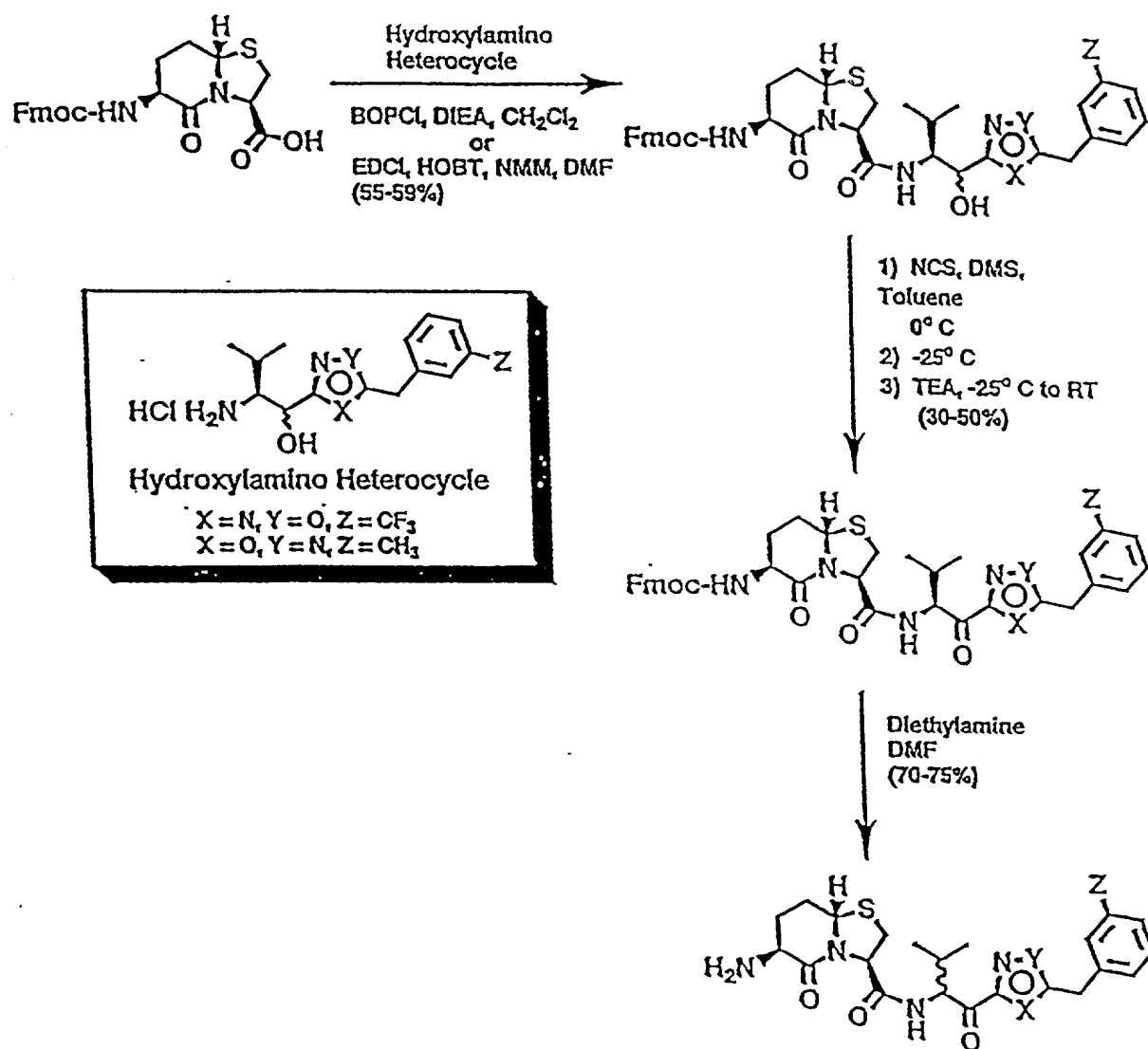
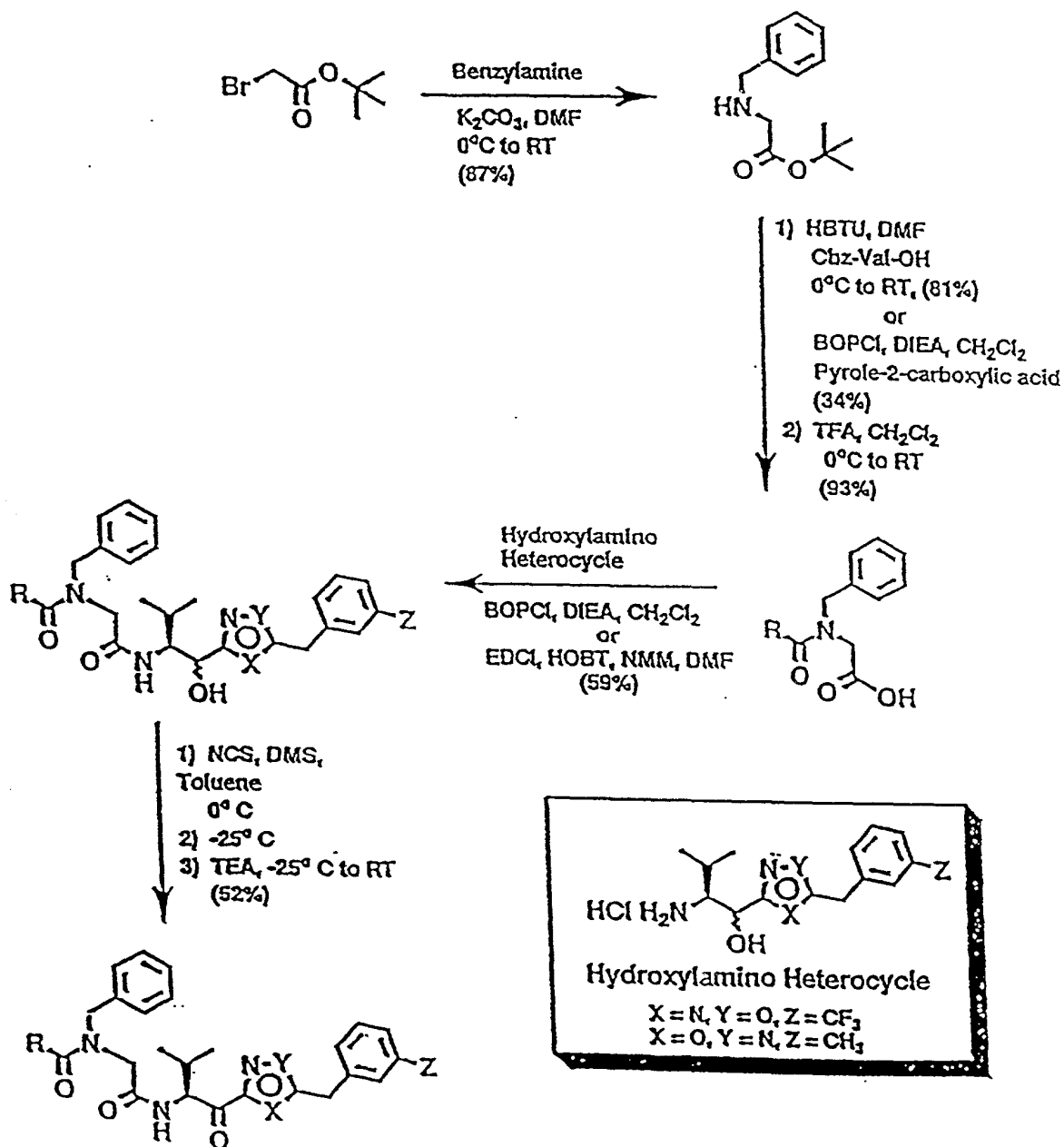


Figure 10

General Synthetic Scheme for P₂-P₃ Modified Inhibitors



20220726-20220726

Figure 11

General Synthetic Scheme for P₂-P₃ Lactam Based Inhibitors

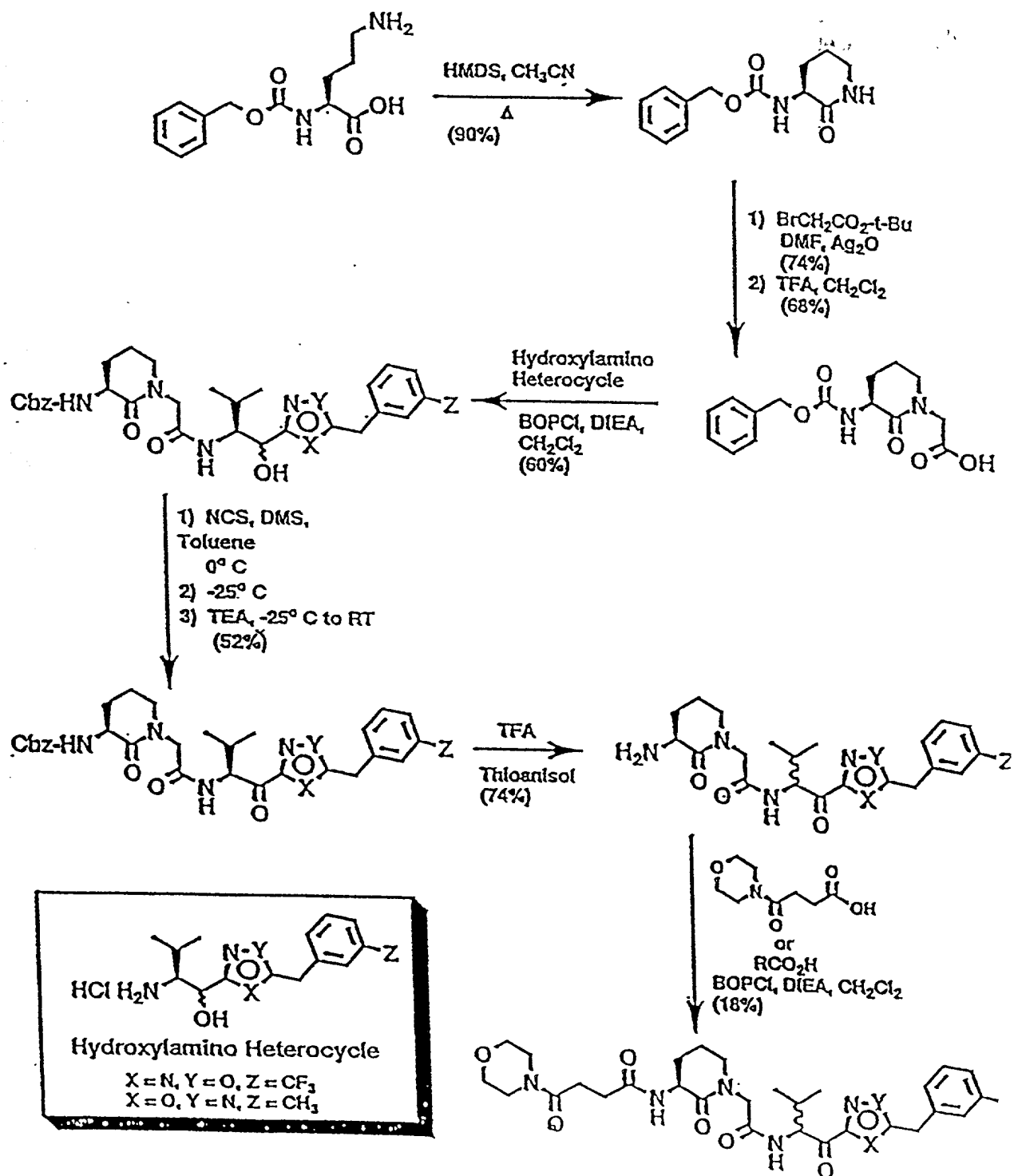
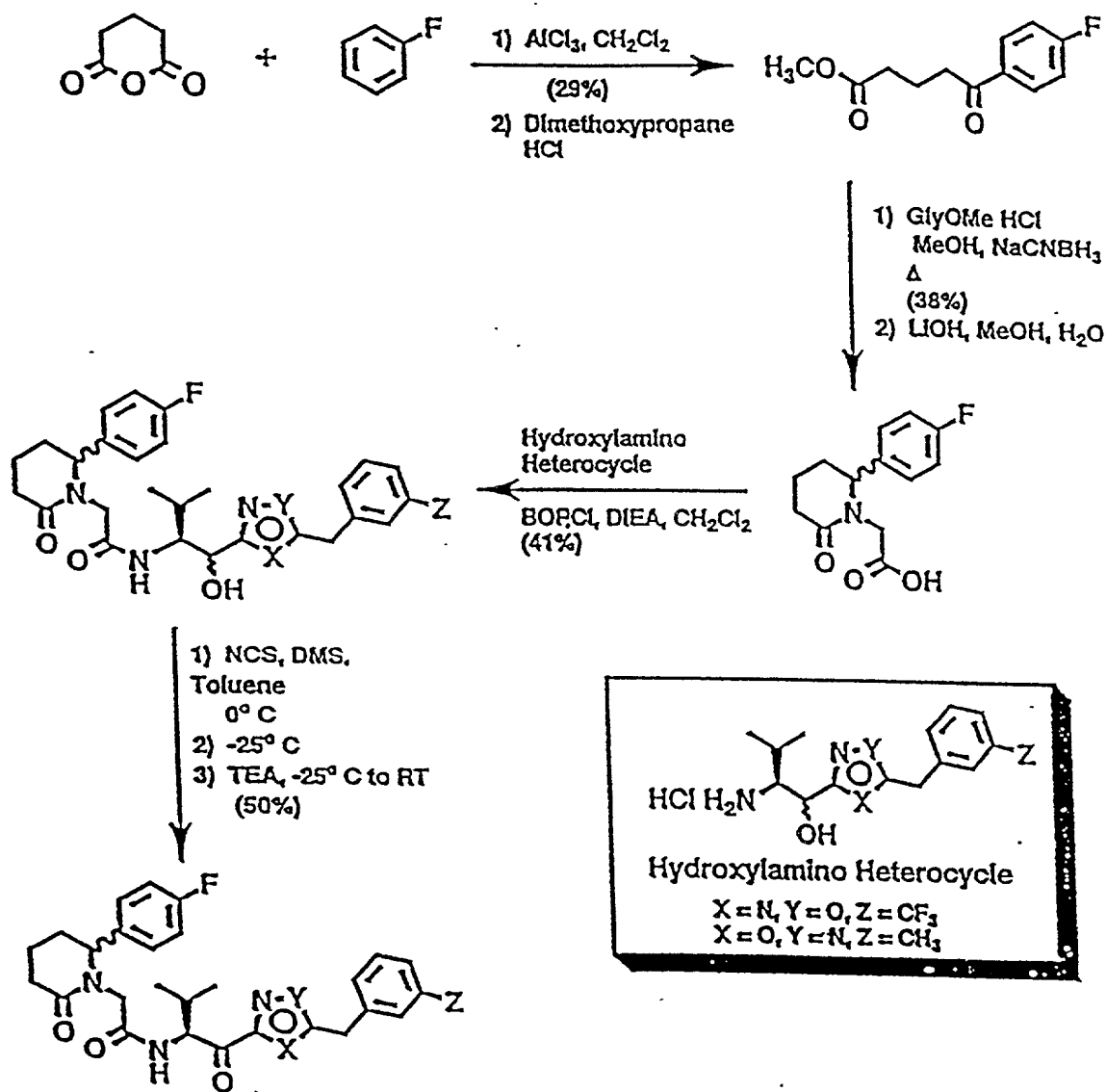


Figure 12

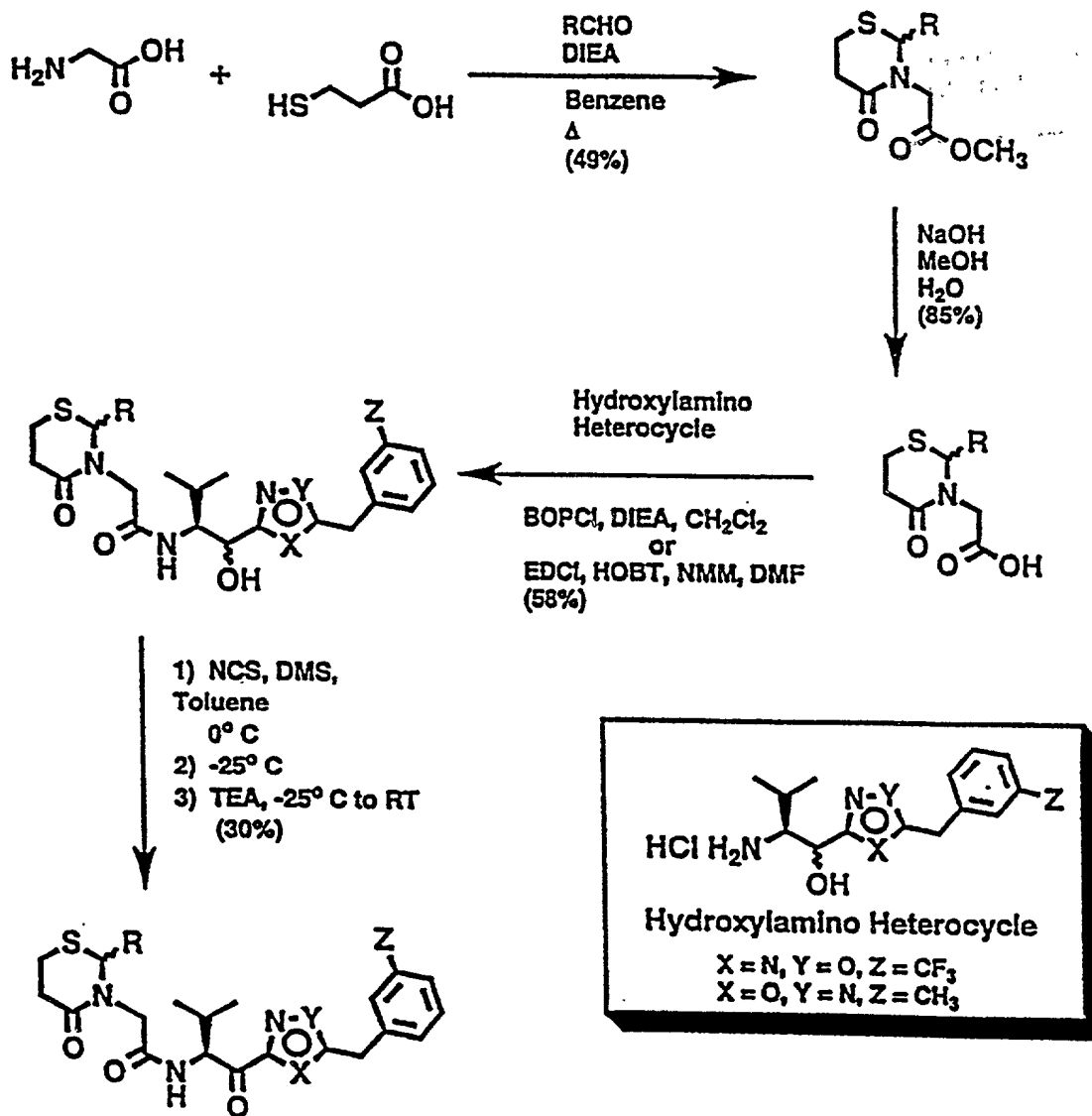
General Synthetic Scheme for P₂-P₃ Lactam Based Inhibitors



2022072822660

Figure 13

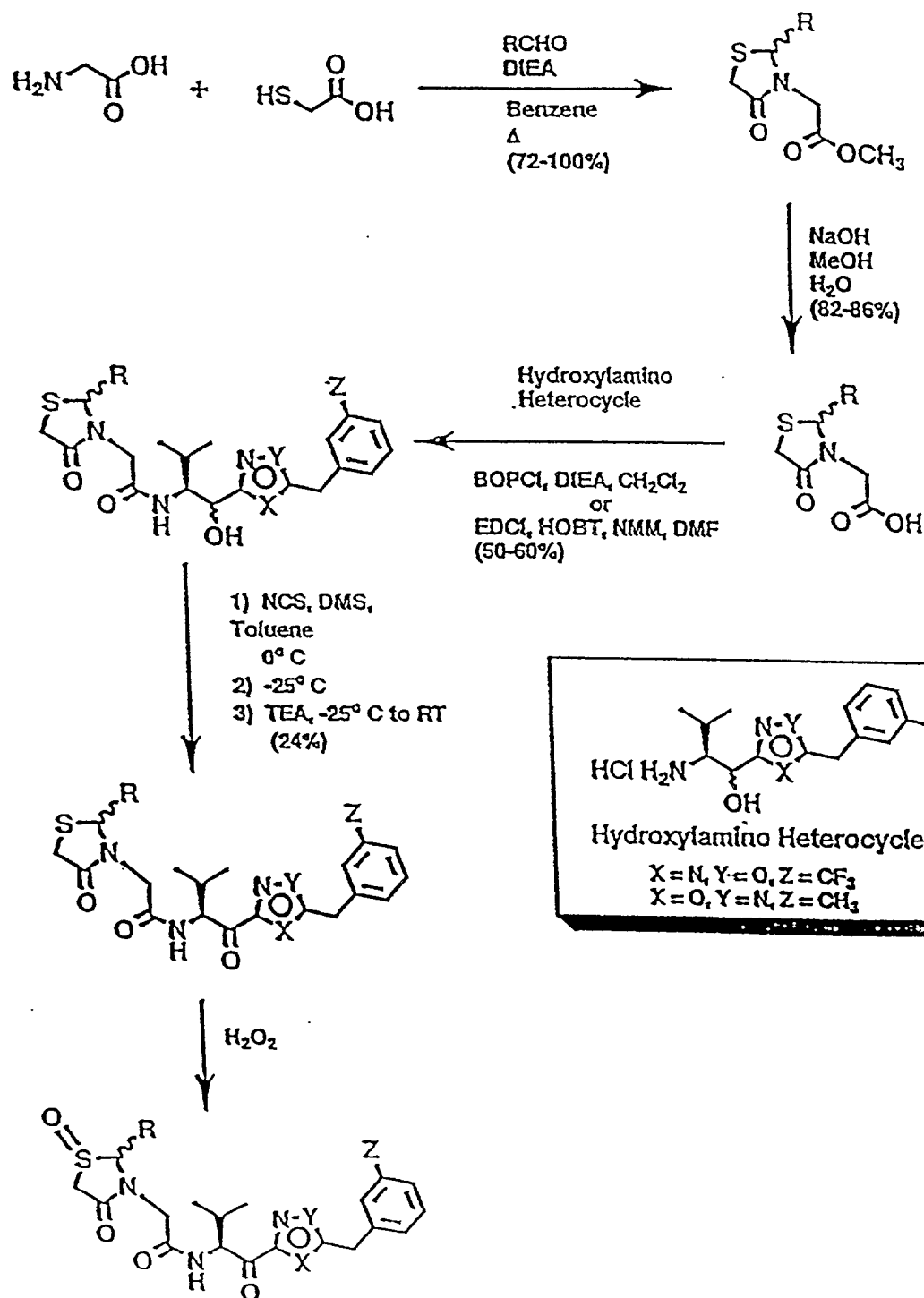
General Synthetic Scheme for Metathiazanone Based Inhibitors



20220728-22220728

Figure 14

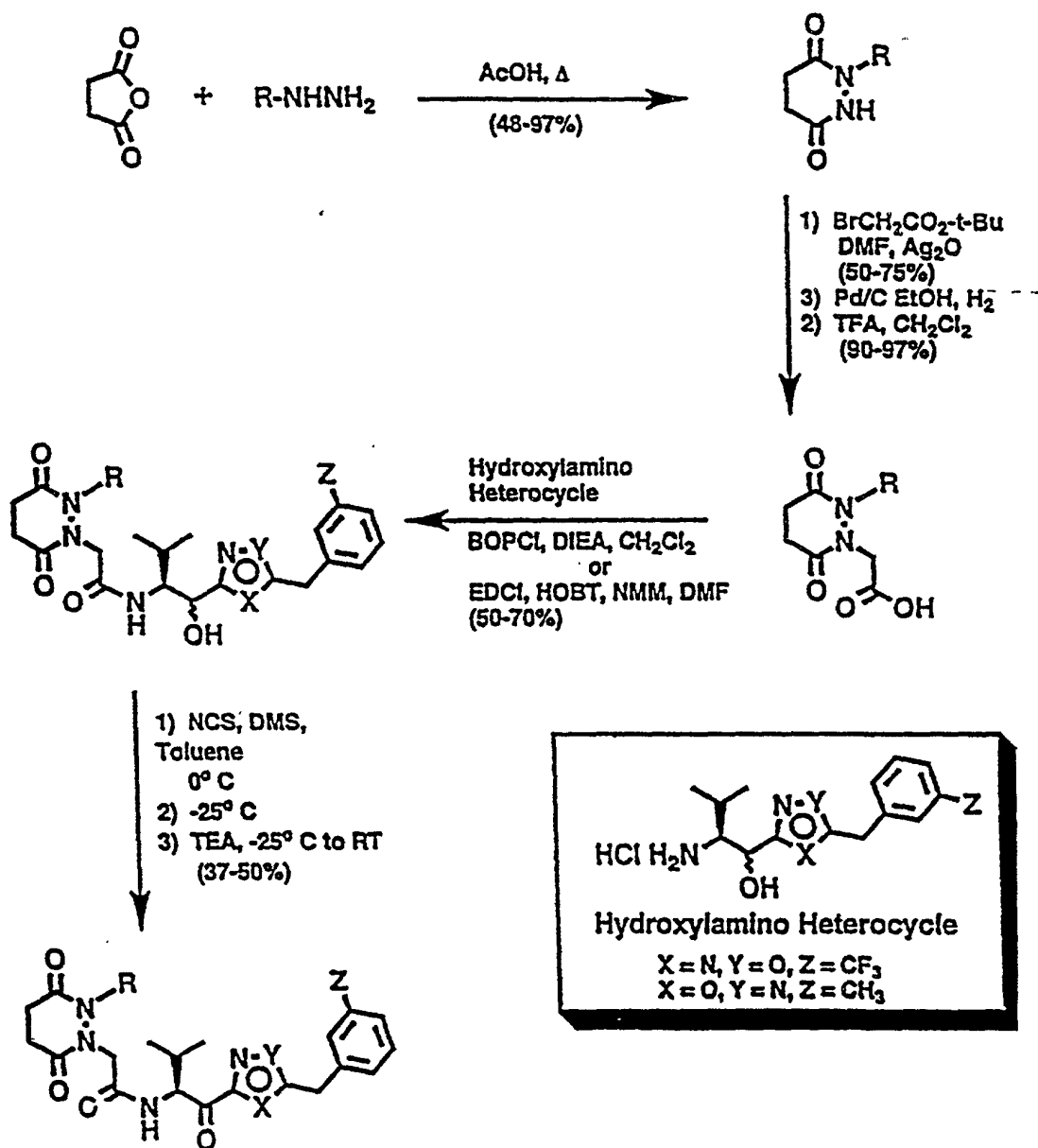
General Synthetic Scheme for Thiazolidinone Based Inhibitors



09927832-02202

Figure 15

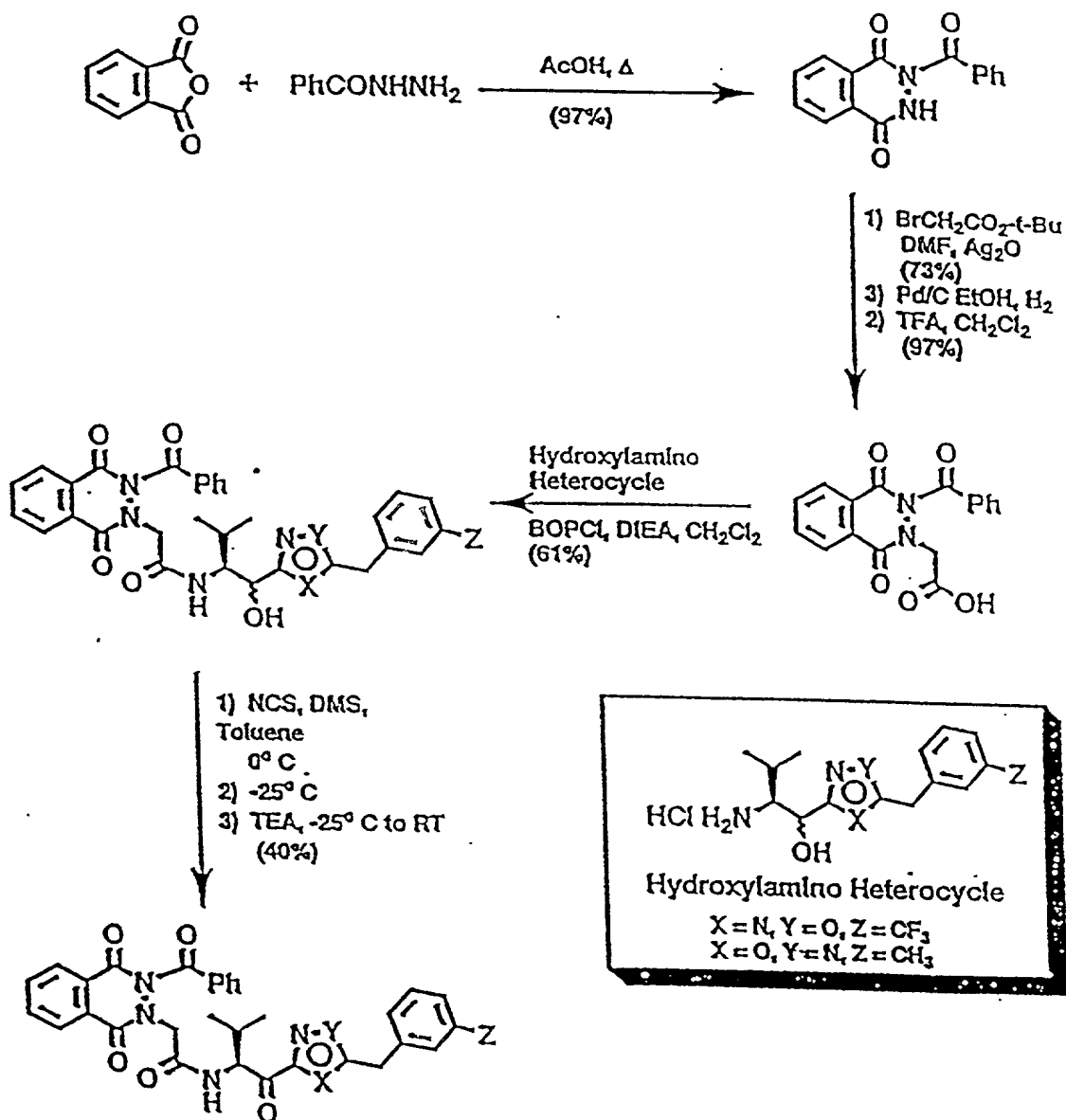
General Synthetic Scheme for Pyridazinedione Based Inhibitors



202220-23/2560

Figure 16

General Synthetic Scheme for Benzopyridazinedione Based Inhibitors



09927833-02200

Figure 17

General Synthetic Scheme for Quinolone and N-Substituted Quinolone Based Inhibitors

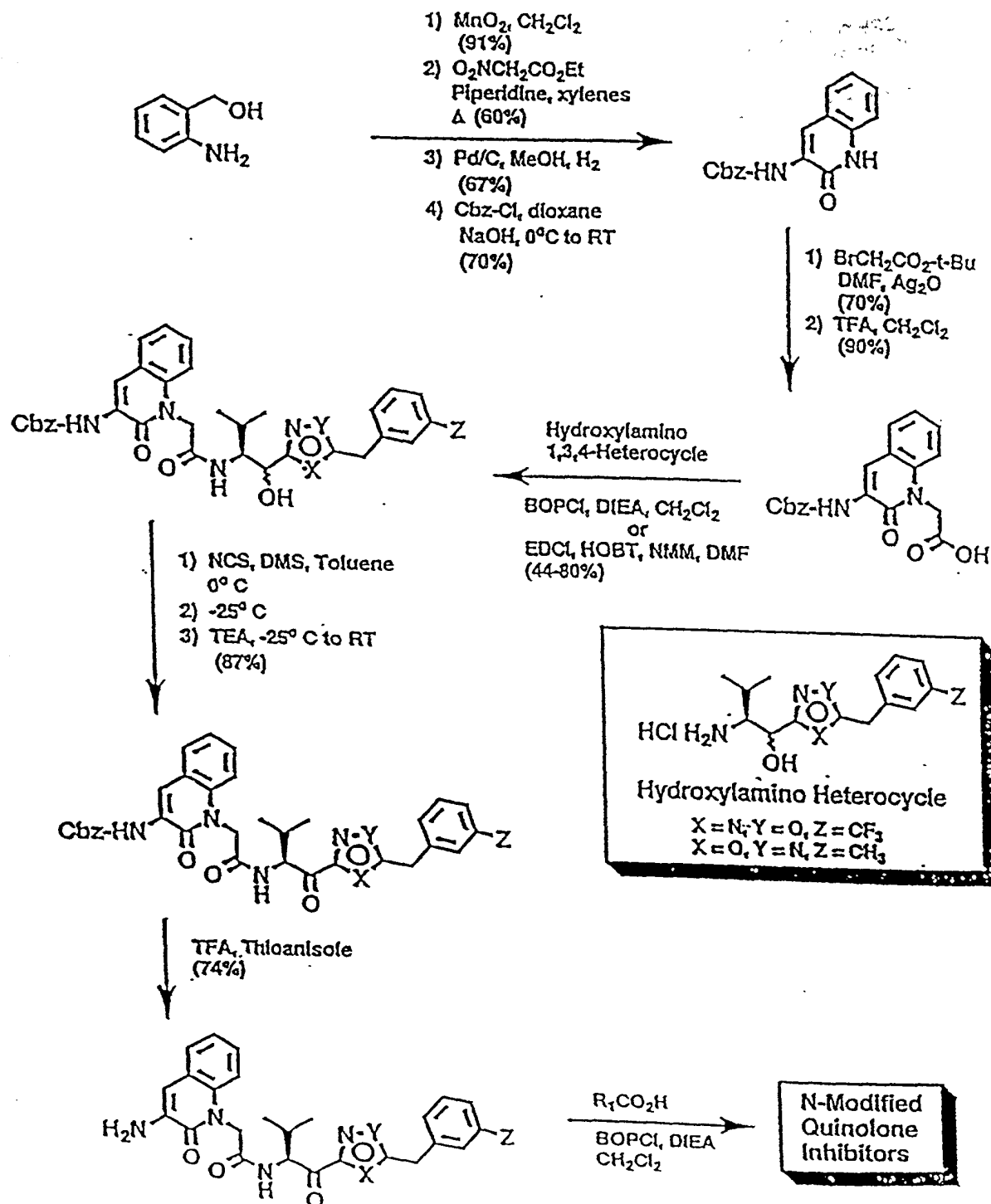
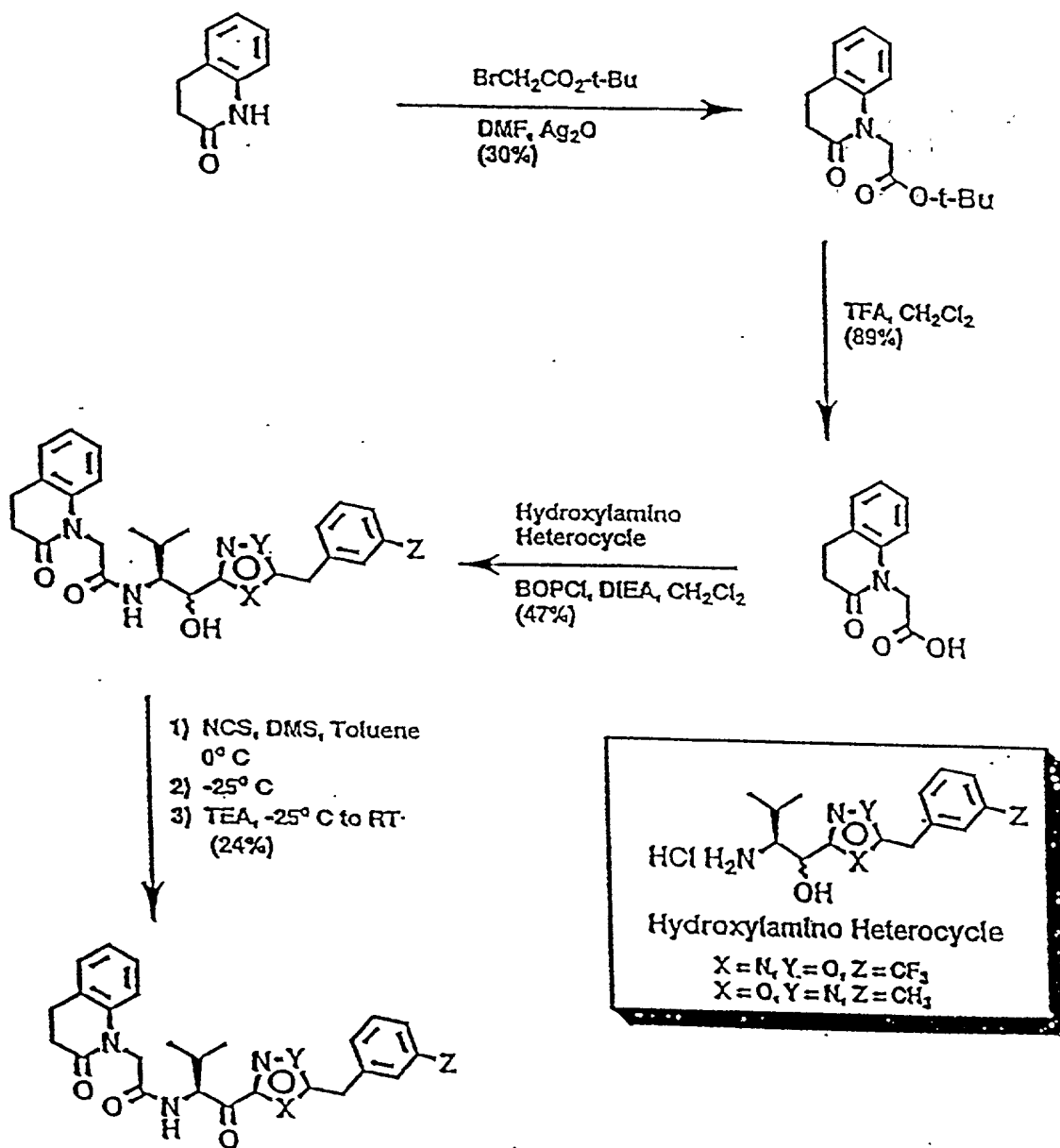


Figure 18

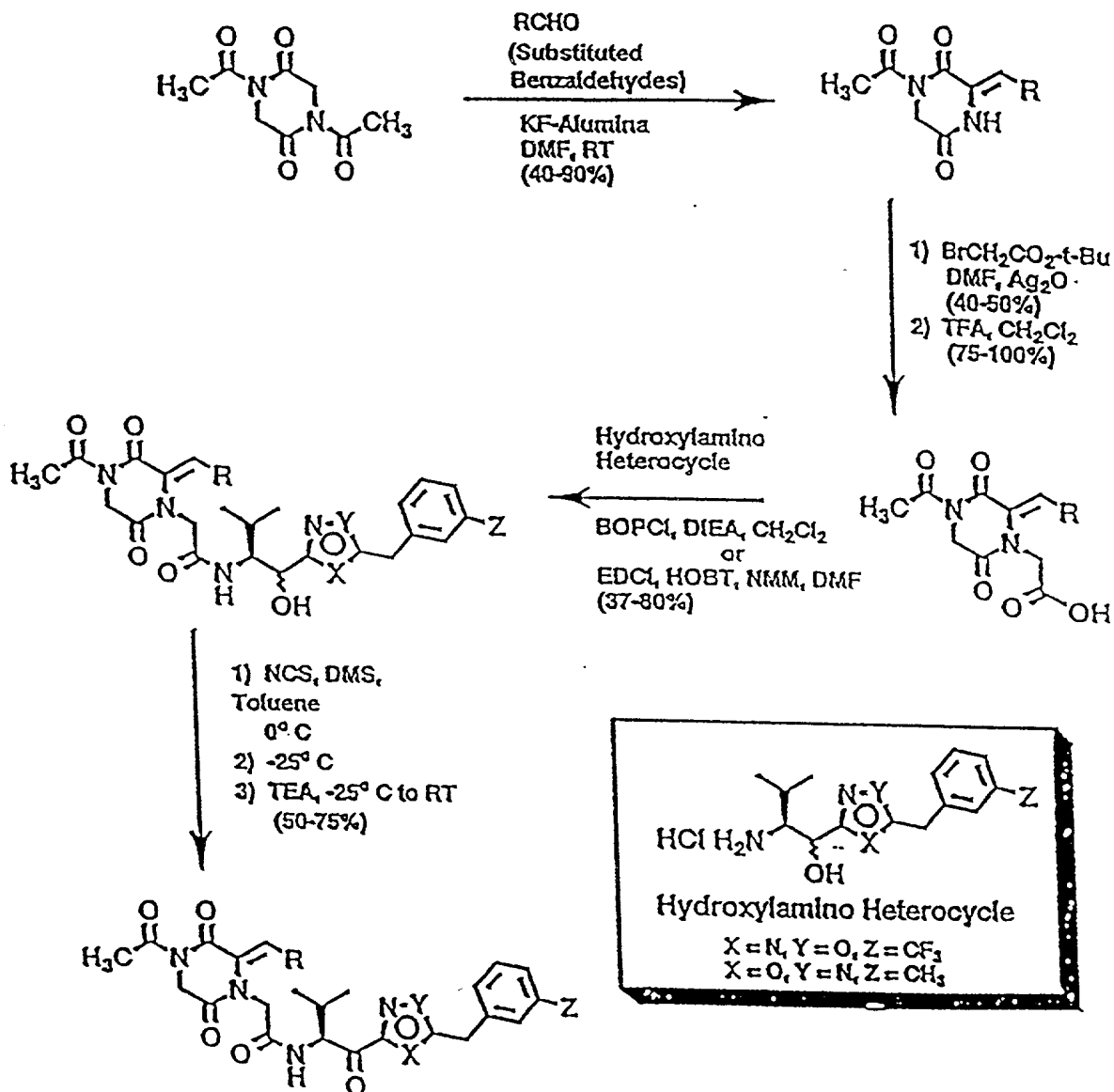
General Synthetic Scheme for 3,4-Dihydroquinolone Based Inhibitors



09927832-02602

Figure 19

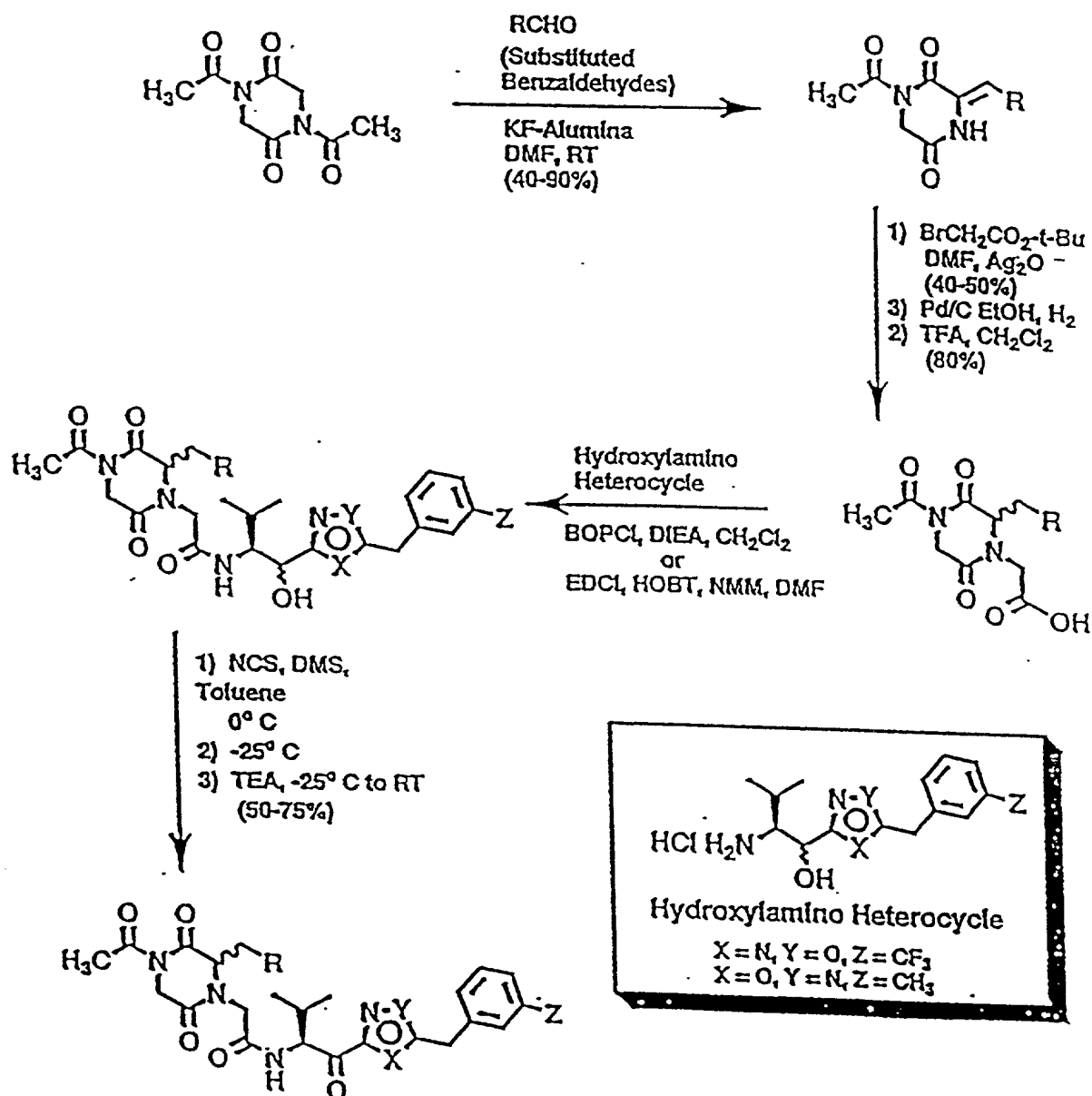
General Synthetic Scheme for Benzylidene Diketopiperazine Based Inhibitors



20220220-22372660

Figure 20

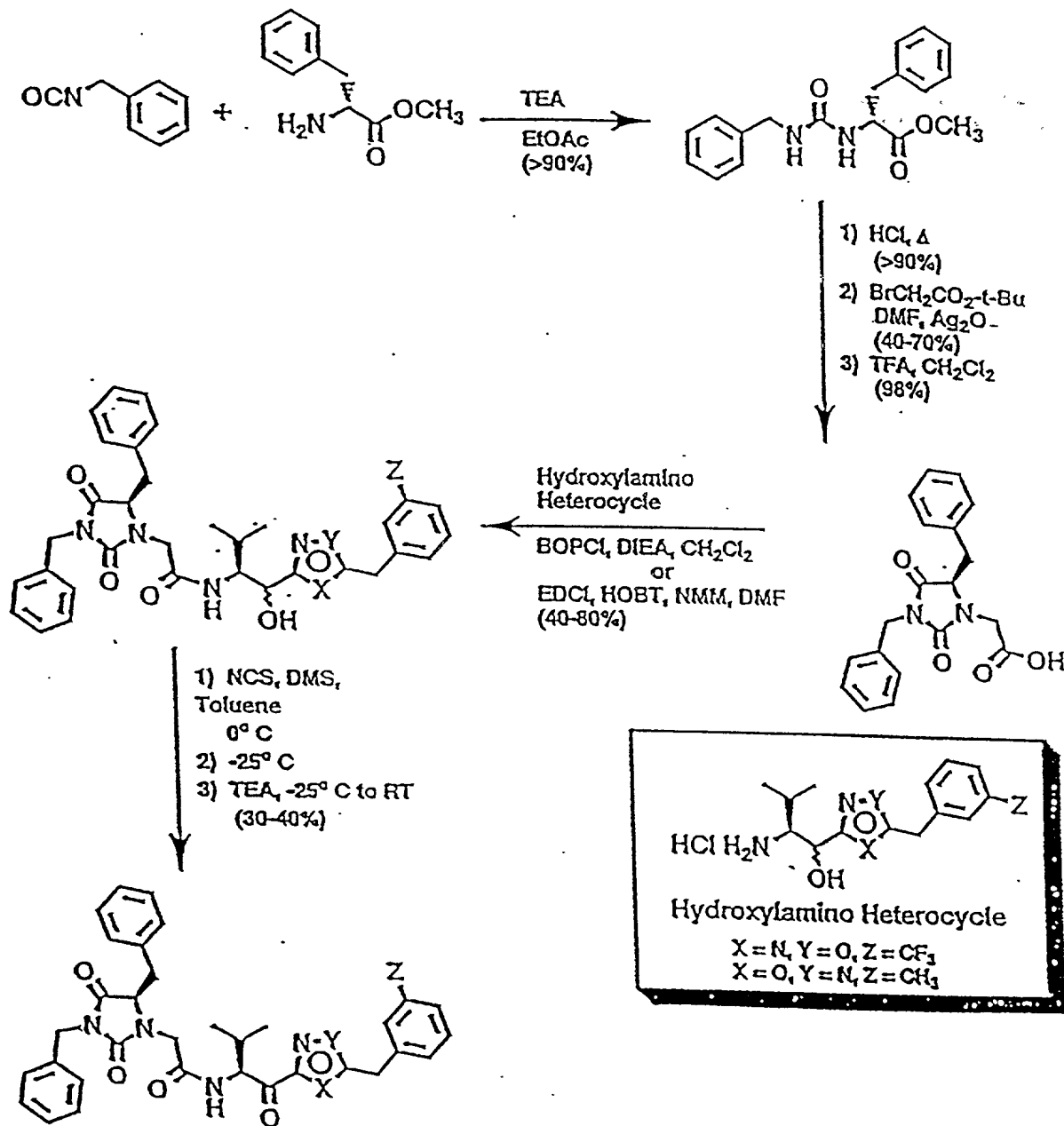
General Synthetic Scheme for Diketopiperazine Based Inhibitors



09927833-02200

Figure 21

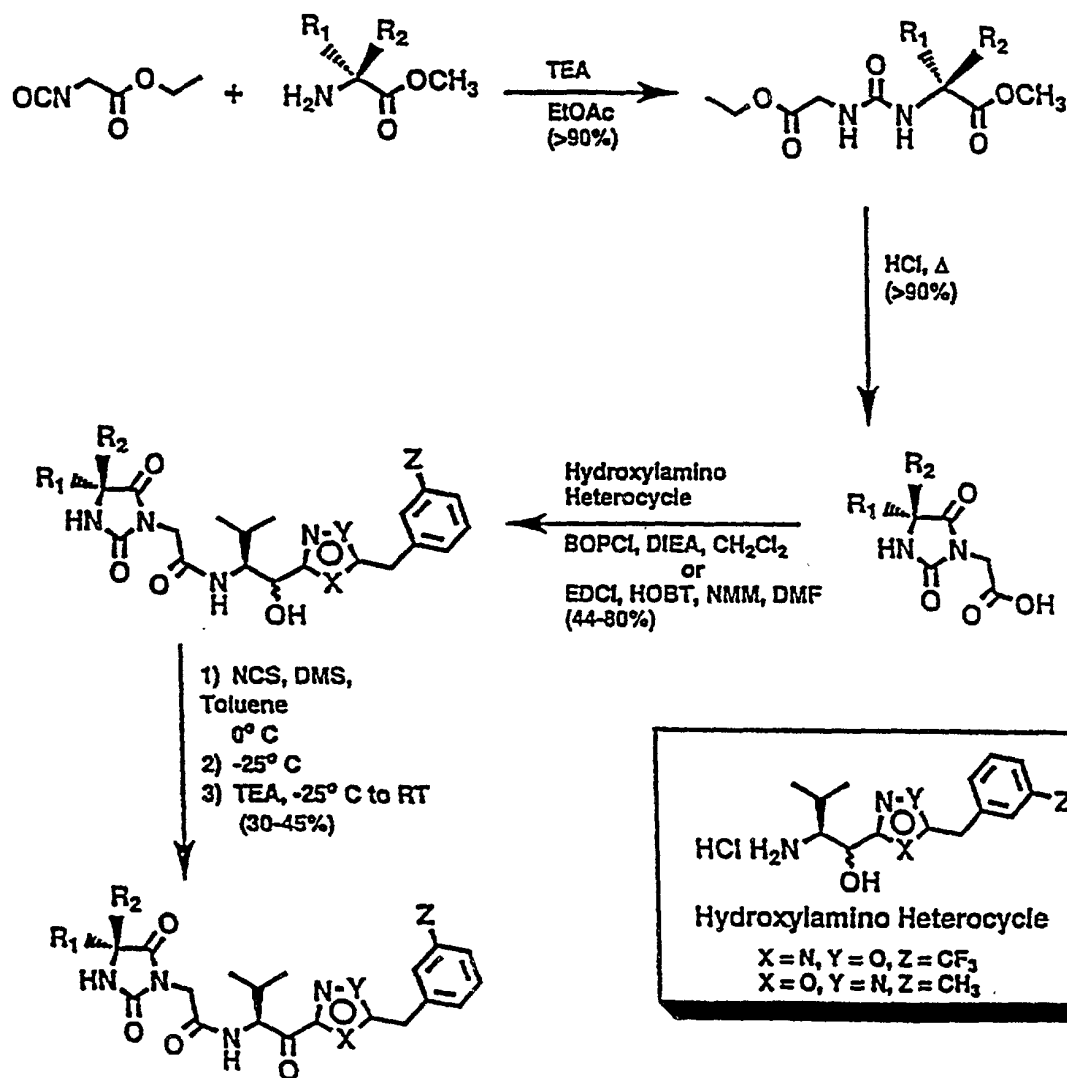
Synthetic Scheme for Hydantoin Based Inhibitors



09627832-02302

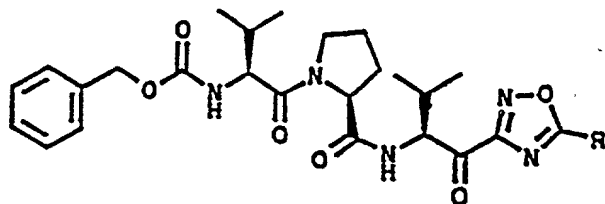
Figure 22

General Synthetic Scheme for Hydantoin Based Inhibitors



09227833-02200

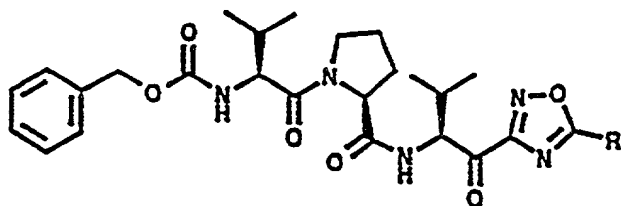
Figure 23



CE#	R	K _i (nM)	CE#	R	K _i (nM)
2039		2.0	2054		0.29
2042		2.5	2055		0.49
2045		1.0	2058		0.56
2048		0.36	2062		0.30
2049		0.5	2066		0.98
2052		0.37	2096		0.8
2053		0.41	2115		1.0

202320-238/23660

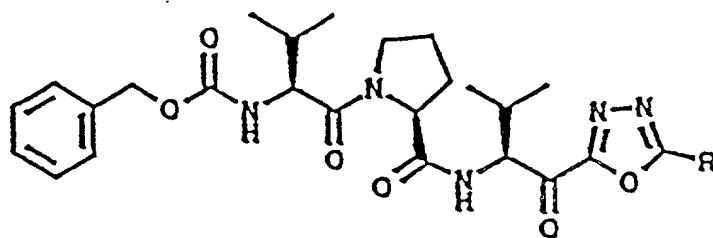
Figure 24



CE#	R	K _i (nM)	CE#	R	K _i (nM)
2046		9.9	2077		0.15
2047		3.8	2078		1.05
2050		1.84	2092		6.3
2057		0.38	2103		12.4
2069		4.4	2119		7.7
2073		0.24	2152		0.24
2076		1.46			

20220-2682660

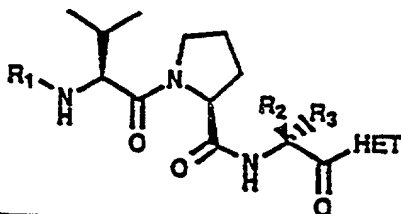
Figure 25



CE#	R	K _i (nM)
2072		0.025
2074	-CH ₃	0.99
2075		0.11
2100		0.069
2123	-N(CH ₃) ₂	15.1
2124		0.033

202220-288/2660

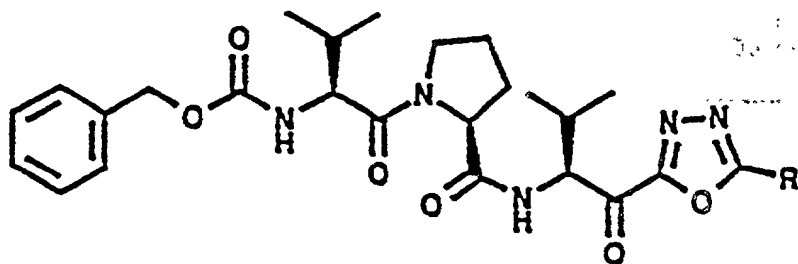
Figure 26



CE#	R ₁	R ₂	R ₃	HET	K _i (nM)
2083	Cbz-	CH ₃	CH ₃		73.0
2098		<i>L</i> -Propyl	H		85.0
2104		<i>L</i> -Propyl	H		0.33
2109		<i>L</i> -Propyl	H		126
2110		<i>L</i> -Propyl	H		0.13

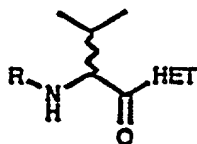
20220220-232650

Figure 27



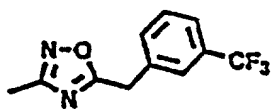
CE#	R	K_i (nM)
2072		0.025
2074	-CH ₃	0.99
2075		0.11
2100		0.069
2123		15.1
2124		0.033

Figure 28

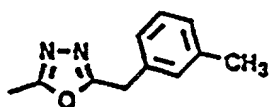


CE#	R	HET	K_i (nM)
2130		B	10.0
2132		A	24.0
2134		B	2.0
2135		A	17
2126		B	5.05
2127		A	33.9

Heterocycles:

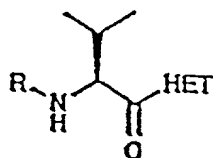


A



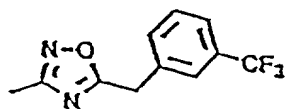
B

Figure 29

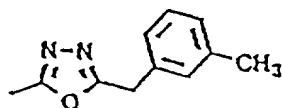


CE#	R	HET	K_i (nM)
2125		A	0.40
2145		B	0.038
2143		A	25.0
2056		A	0.98
2097		A	60.0
2156		A	512.0

Heterocycles:

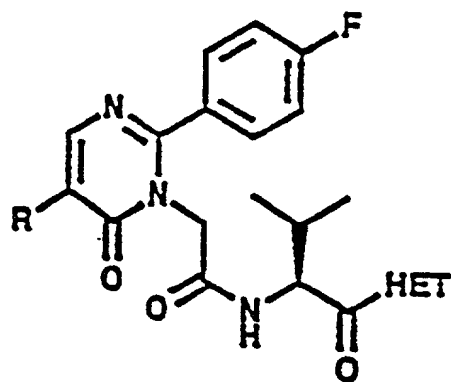


A



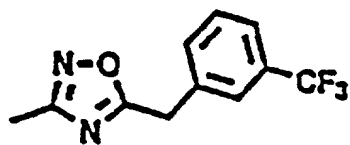
B

Figure 30

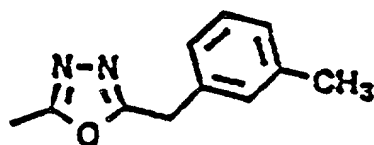


CE#	R	HET	K_i (nM)
2089	Cbz-NH-	A	1.5
2090	NH ₂	A	2.7
2095	Cbz-NH-	B	0.21
2101	NH ₂	B	0.64

Heterocycles:

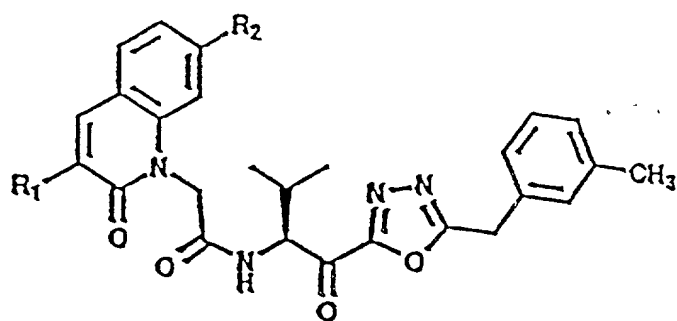


A

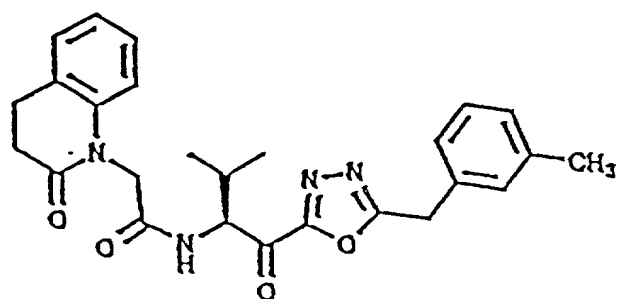


B

Figure 31

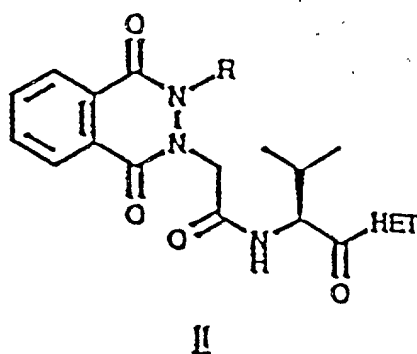
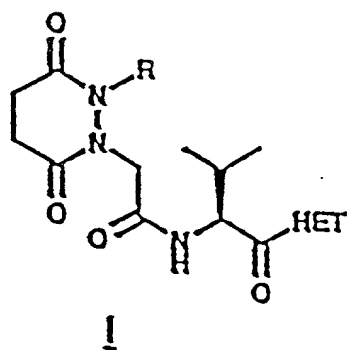


CE#	R_1	R_2	K_I (nM)
2107	Cbz-NH-		17.0
2108	Cbz-NH-	H	10.5
2113	H ₂ N-	H	38.8
2116		H	76.3
2117		F	587.0



CE-2088 $K_I = 66.0$ nM

Figure 32



CE#	R	Structure	HET	K _i (nM)
2138		I	B	294.0
2147		I	B	1590
2148		I	A	>6000
2140		II	B	204.4

Heterocycles:

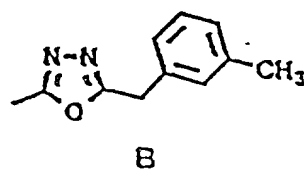
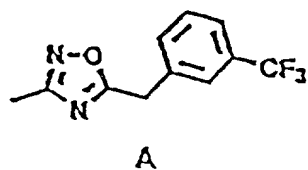
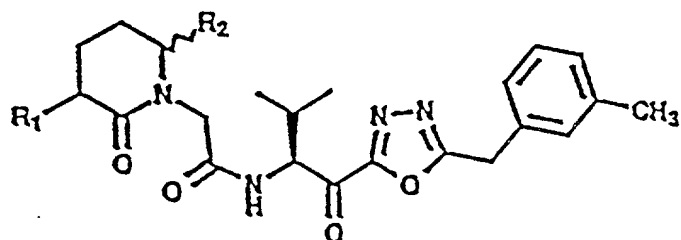

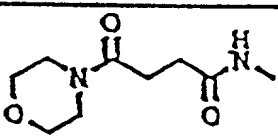


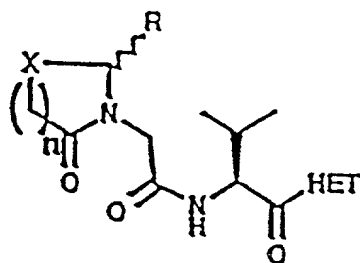
Figure 33



CE#	R ₁	R ₂	K _i (nM)
2079	Cbz-NH-	H	35.5
2080	H ₂ N-	H	62.0
2087	H		19.8
2091		H	270.0

202220-228/22660

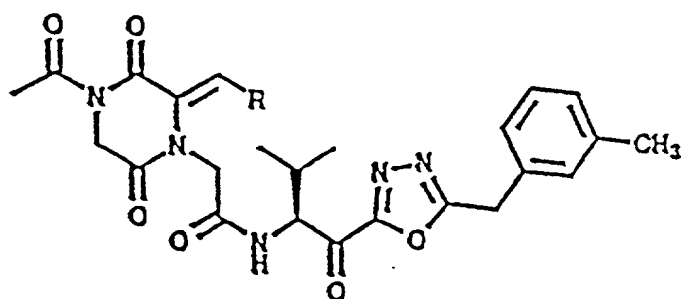
Figure 34



CE#	n	X	HET	R	K _i (nM)
2118	2	S			13.2
2121	1	S			28.0
2122	1	S			62.7
2136	1	SO			104.0
2137	1	SO			557.0

20220123-2382660

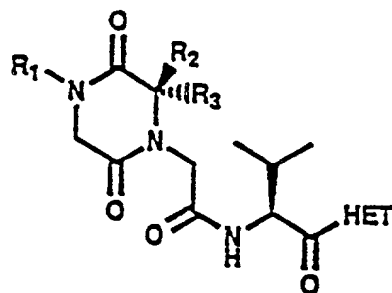
Figure 35



CE#	R	K _i (nM)
2099		1.9
2105		0.72
2111		20.1
2112		1.17
2114		25.1

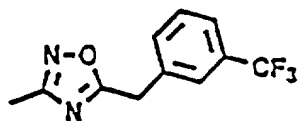
20220728/22660

Figure 36

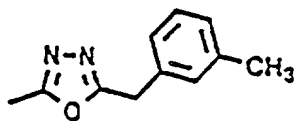


CE#	R ₁	R ₂	R ₃	HET	K _i (nM)
2084	CH ₃			A	133.0
2106	CH ₃			B	40.7
2120	CH ₃ CO-			B	50.9
2128				B	64.0
2129				A	300.3
2133				C	33200
2139	H-			B	41.0
2144				B	9.3
2146				A	67.3

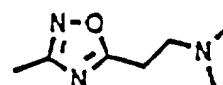
Heterocycles:



A

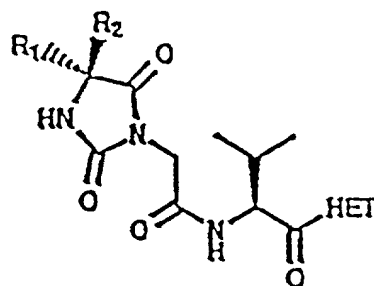


B



C

Figure 37



CE#	R ₁	R ₂	HET	K _i (nM)
2141		H	A	64.0
2142		H	B	8.7
2149 **		H	B	0.28
2154	H		B	10.0
2155	H		A	57.0

** Stereochemistry not definitive

Heterocycles:

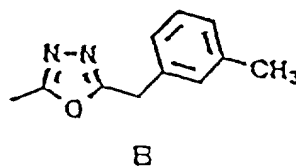
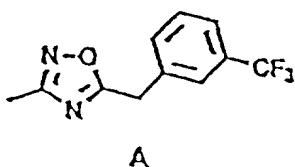
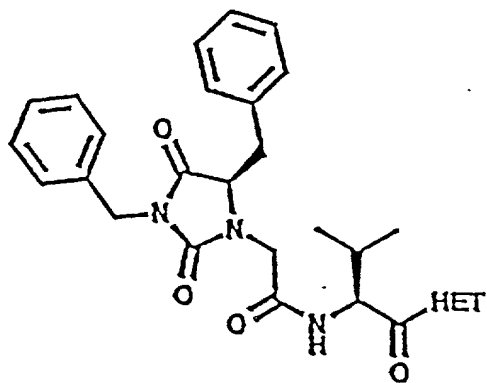


Figure 38



CE#	HET	K_i (nM)
2150		>1000
2151		60

202220-28272660

